EXAMINER'S AMENDMENT

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Scott Kamholz on December 13, 2009.

The application has been amended as follows:

AMENDMENTS TO THE SPECIFICATION

Amend paragraph [40], which starts on p. 13, as follows:

--**[40]** A substantially rigid frame **50** may be provided to hold the flexible tubule **10** suitably ~~taught~~ taut by constraining at least the ~~two~~ proximal and distal ends of the tubule. In an exemplary embodiment, a first constraint may be provided to permanently attach and seal the tubule to the frame around the first opening of the tube. This seal may be created by welding the flexible tubule to the frame using thermal and/or ultrasonic sources. Alternatively, the seal may be created using a hot-melt adhesive joint with ethylene vinyl acetate, or by making a joint using a UV cure epoxy or other adhesives. In further embodiments, the tubule may be mechanically sealed or insert-molded with the frame. A second constraint may be provided to attach and seal the tubule to the base of the frame. In an exemplary embodiment of this second constraint, this end of the tubule may be sealed flat and attached to the rigid frame by thermal and/or ultrasonic welding techniques. Alternatively, this joint and seal may also be formed using adhesive or mechanical approaches. In an alternative embodiment, the second seal may be similar to the first seal, being substantially open to enable access to the contents of the flexible tubule from the second opening. The tubule and frame materials can be optimized for joint manufacture. For

example, the frame can be made of polypropylene having a lower melting point than the thinner tubule to ensure more uniform melting across one or more weld zones. To facilitate welding between the tubule and the frame, the joint area may be tapered or otherwise shaped to include energy directors or other commonly used features enhance weld performance. In an exemplary embodiment, the rigid frame can be made of any suitable plastic by injection molding with its dimensions being approximately 150 mm tall by 25 mm wide.--

Amend paragraph [41], which starts on p. 14, as follows:

--**[41]** The rigid frame **50** can incorporate several features to facilitate the compression and flattening of the flexible tubule. For example, in an exemplary embodiment, the flexible tubule **10** may be constrained only at its two axial extremities to allow maximum radial freedom to avoid encumbering the tubule's radial movement as it is compressed. In another embodiment, compression may be facilitated by including a relief area in the frame, near the first opening of the tube. This relief area may be used to facilitate the flexible tubule's transition from a substantially compressed shape in the tubule segments to a substantially open shape at the first opening. Other useful features of the rigid frame that can facilitate flexible tubule compression may include an integral tubule tensioning mechanism. In an exemplary embodiment, this tension mechanism could be manufactured by molding features such as cantilever or leaf type springs directly into the rigid frame to pull the tubule ~~taught~~ taut at one of its attachment points with the frame.--

AMENDMENTS TO THE CLAIMS

1. **(Currently amended)** A sample processing apparatus, comprising:

a tubule, comprising:

a proximal end having an opening through which a sample is introducible;

a distal end; and

at least a first segment containing at least one substance capable of specific binding to a preselected component of a sample when the sample is added to the tubule, a second segment distal to the first segment and containing a wash reagent, and a third segment distal to the second segment and containing an amplification reagent, each of which segments is:

defined by the tubule;

fluidly isolated, at least in part by a fluid-tight seal formed by a bonding of opposed wall portions of the tubule to one another such that:

(a) the seal is broken by application of fluid pressure on a segment that is fluidly isolated in part by the seal; and

(b) the seal is capable of being clamped where the opposed wall portions of the tubule are bonded, without breaking the seal, to prevent the seal from being broken by application of fluid pressure on a segment that is fluidly isolated in part by the seal;

so expandable as to receive a volume of fluid expelled from another segment; and

so compressible as to contain substantially no fluid when so compressed;

a cap for closing the opening, the cap containing a chamber in fluid communication with the tubule, and the cap permitting free escape of gasses but retaining all liquid volumes and infectious agents in the tube;

a rigid frame to which the tubule's proximal and distal ends are held; and

an integral tubule tensioning mechanism or an attachment of the tubule to the frame that pulls the tubule sufficiently taut so as to facilitate compression and flattening of the tubule.

2. (**Currently amended**) The ~~tubule~~ apparatus of claim 1, wherein at least a portion of the tubule is transparent.

3. (**Currently amended**) The ~~tubule~~ apparatus of claim 1, further comprising at least one pressure gate in fluid communication with at least one segment.

4. (**Currently amended**) The ~~tubule~~ apparatus of claim 1, further comprising at least one filter in the tubule.

5. (Canceled)

6. (**Currently amended**) The ~~tubule~~ apparatus of claim 1, wherein the preselected component is nucleic acid.

7. (**Currently amended**) The ~~tubule~~ apparatus of claim 6, wherein the substance capable of specific binding to nucleic acid includes at least one of an antibody, nucleic acid, peptide

nucleic acid, phosphothioate nucleic acid, silica coated surface, electrostatically charged surface, and enzyme.

8. **(Currently amended)** The ~~tubule~~ apparatus of claim 7, wherein the substance capable of specific binding to nucleic acid has a preselected amino acid or base sequence.

9. **(Currently amended)** The ~~tubule~~ apparatus of claim 1, wherein the substance comprises at least one of a receptor, a ligand, an antibody, an antigen, a nucleic acid probe, a peptide nucleic acid probe, a phosphothioate nucleic acid probe, a bacteriophage, silica, and an electrostatic charged surface.

10. **(Currently amended)** The ~~tubule~~ apparatus of claim 1, wherein the substance is capable of specific binding to a preselected component of at least one of bacteria, virus, parasite, cells, nucleic acid, and spores.

11. **(Withdrawn -- Currently amended)** The ~~tubule~~ apparatus of claim 10, wherein the substance is capable of specific binding to a preselected component of at least one of *Yersinia pestis, Francisella tularensis, Listeria monocytogenes, Bacillus anthracis, Escherichia coli, Salmonella enteritidis, Campylobacter pylori, Campylobacter jejuni Clostridium perfringens, Staphylococcus aureus, Haemophilus influenzae, Streptococcus pneumoniae, Neisseria meningitides, Vibrio cholerae, Mycobacterium tuberculosis, and Mycobacterium leprae.*

12. **(Withdrawn -- Currently amended)** The ~~tubule~~ apparatus of claim 10, wherein the substance is capable of specific binding to a preselected component of at least one of human immunodeficiency virus 1, human immunodeficiency virus 2, influenza virus,

yellow fever virus, dengue virus, hepatitis B virus, hepatitis C virus, cytomegalovirus, Epstein Barr virus, West Nile virus, hantavirus, and small pox.

13. **(Withdrawn -- Currently amended)** The ~~tubule~~ apparatus of claim 10, wherein the substance is capable of specific binding to a preselected component of at least one of *Plasmodium falciparum, Plasmodium vivax, Plasmodium ovale, Plasmodium malariae, Leishmania tropica, Leishmania donovani, Leishmania infantum, Leishmania major, Leishmania mexicana, Leishmania chagasi, Leishmania brasiliensis, and Leishmania amazoniensis*.

14. **(Currently amended)** The ~~tubule~~ apparatus of claim 1, wherein the substance capable of specific binding to a preselected component of a sample is coupled to a solid substrate.

15. **(Currently amended)** The ~~tubule~~ apparatus of claim 14, wherein the substance forms a coating on the solid substrate.

16. **(Currently amended)** The ~~tubule~~ apparatus of claim 14, wherein the solid substrate comprises at least one of beads, a pad, a filter, a sheet, an electrostatic surface, and a portion of a tubule wall surface.

17. **(Currently amended)** The ~~tubule~~ apparatus of claim 14, wherein the substrate comprises at least one of silica beads, magnetic beads, silica magnetic beads, glass beads, nitrocellulose colloid beads, and magnetized nitrocellulose colloid beads.

18. **(Currently amended)** The ~~tubule~~ apparatus of claim 14, wherein the substance comprises silica, and the substrate comprises a filter or a sheet.

19. **(Withdrawn -- Currently amended)** The ~~tubule~~ apparatus of claim 14, wherein the substrate comprises a pad formed at least in part from an absorbent material comprising at least one of paper, film, filter, foam, mesh, and fiber matrix.

20. **(Withdrawn -- Currently amended)** The ~~tubule~~ apparatus of claim 14, wherein the substrate is coupled to a tubule wall.

21. **(Withdrawn -- Currently amended)** The ~~tubule~~ apparatus of claim 1, further comprising a solid substrate which comprises a pad formed at least in part from an absorbent material comprising at least one of paper, film, filter, foam, mesh, and fiber matrix.

22. (Canceled)

23. **(Canceled)**

24. **(Currently amended)** The ~~tubule~~ apparatus of claim ~~23,~~ 1, wherein the cap comprises a sample collection device including at least one of a swab, a stick, a scoop, an inoculation loop, a forceps, a dropper, a capillary tube, and a syringe.

25. **(Currently amended)** The ~~tubule~~ apparatus of claim 24, wherein the sample collection device is so disposed in or on the cap as to transfer a sample from the device to the tubule when the cap is positioned in relation to the tubule to close the open end of the tubule.

26. **(Canceled)**

27. **(Currently amended)** The ~~tubule~~ apparatus of claim ~~23,~~ 1, wherein the cap comprises a member defining the chamber, and wherein the chamber is ~~an~~ expandable ~~chamber in the cap~~.

28. **(Currently amended)** The ~~tubule~~ apparatus of claim 27, wherein a cap wall defines a vent.

29. **(Canceled)**

30. **(Currently amended)** The ~~tubule~~ apparatus of claim ~~29,~~ 1, wherein the frame comprises an interface, the interface receiving the proximal end of the tubule.

31. **(Currently amended)** The ~~tubule~~ apparatus of claim 30, wherein the interface also receives ~~a~~ the cap, thereby sealing the proximal end of the tubule.

32. **(Currently amended)** The ~~tubule~~ apparatus of claim 1, further comprising at least one of a diluent, suspension reagent, lysis reagent, neutralization reagent, elution reagent, proteolytic reagent, glycosylase, nucleic acid, nuclease, ligase, alcohol, reverse transcription reagent, and germination reagent.

33. **(Withdrawn -- Currently amended)** The ~~tubule~~ apparatus of claim 32, wherein the tubule comprises an elution reagent that includes at least one of Tris buffer, water, and buffer suitable for polymerase chain reaction.

34. **(Withdrawn -- Currently amended)** The ~~tubule~~ apparatus of claim 32, wherein the tubule comprises a lysis reagent that includes at least one of a guanidinium salt, a chaotropic salt, a red blood cell lysis reagent, a detergent, a chelator, a spore germination reagent, sodium hydroxide, proteinase K, DNase inhibitor, RNase, RNase inhibitor, anticoagulant, coagulant, a protease, a germinant solution, and a surfactant.

35. (**Withdrawn -- Currently amended**) The ~~tubule~~ apparatus of claim 32, wherein the tubule comprises a germination reagent including heart brain infusion medium and at least one of L-alanine, inosine, L-phenylalanine, L-Serine and L- proline.

Claims 36-43 (Canceled)

44. (**Currently amended**) The ~~tubule~~ apparatus of claim 1, wherein the segments form a substantially linear array.

45. (**Currently amended**) The ~~tubule~~ apparatus of claim 1, wherein the segments form a contiguous array.

46. (Canceled)

47. (**Currently amended**) A sample processing apparatus, comprising:

a tubule, comprising:

a plurality of segments, each of which is:

defined by the tubule;

fluidly isolated, at least in part by a fluid-tight seal formed by a bonding of opposed wall portions of the tubule to one another such that:

(a) the seal is broken by application of fluid pressure on a segment that is fluidly isolated in part by the seal; and

(b) the seal is capable of being clamped where the opposed wall portions of the tubule are bonded, without breaking the seal, to prevent the seal from being broken by application of fluid pressure on a segment that is fluidly isolated in part by the seal;

separated from adjacent segments only by seals;

so expandable as to receive a volume of fluid expelled from another segment; and

so compressible as to contain substantially no fluid when so compressed;

wherein:

a segment contains at least one of a lysis reagent and a diluent;

a segment contains at least a nucleic acid binding reagent;

a segment contains at least a wash reagent;

a segment contains at least a nucleic acid eluting regent; and

a segment contains at least nucleic acid amplification reagents;

a cap for closing the opening, the cap containing a chamber in fluid communication with the tubule, and the cap permitting free escape of gasses but retaining all liquid volumes and infectious agents in the tube;

a rigid frame to which the tubule's proximal and distal ends are held; and

an integral tubule tensioning mechanism or an attachment of the tubule to the frame that pulls the tubule sufficiently taut so as to facilitate compression and flattening of the tubule.

Claims 48-75 (Canceled)

76. **(Currently amended)** The ~~tubule~~ apparatus of claim 1, wherein at least one of the reagents is in a dry format.

77. (Canceled)

78. **(Currently amended)** The ~~tubule~~ apparatus of claim ~~77,~~ 94, wherein the segments form a substantially linear array.

79. **(Currently amended)** The ~~tubule~~ apparatus of claim 78, wherein the segments form a contiguous array.

80. **(Currently amended)** The ~~tubule~~ apparatus of claim 1, wherein the segments form a contiguous and substantially linear array.

Claims 81-84 (Canceled)

85. **(Currently amended)** The ~~tubule~~ apparatus of claim 1, further comprising at least a fourth segment that (a) is distal to the second segment and (b) contains at least one of an elution reagent, second wash regent, lysis reagent, reverse transcription reagent, a nucleic acid, a nuclease, and glycosylase.

86. **(Currently amended)** The ~~tubule~~ apparatus of claim 1, further comprising at least a fourth segment that (a) is proximal to the first segment and (b) contains at least one of a

germination reagent, suspension reagent, lysis reagent, neutralization reagent, diluent, second wash reagent, elution reagent, nucleic acid, and proteolytic reagent.

87. **(Currently amended)** The ~~tubule~~ apparatus of claim 1, further comprising at least a fourth segment that (a) is distal to the third segment and (b) contains at least one of a second amplification reagent, a nuclease, a detection reagent, and a glycosylase.

88. **(Currently amended)** The ~~tubule~~ apparatus of claim 1, further comprising at least a fourth segment that (a) is distal to the first segment and (b) contains at least one of a diluent, suspension reagent, nucleic acid, lysis reagent, second wash reagent, a solid substrate, and alcohol.

89. **(Currently amended)** The ~~tubule~~ apparatus of claim 1, further comprising:

a fourth segment that (a) is proximal to the first segment and (b) contains at least one of a lysis reagent and a diluent; and

a fifth segment that (a) is distal to the second segment, (b) proximal to the third segment, and (c) contains an elution reagent.

90. **(Currently amended)** The ~~tubule~~ apparatus of claim 1, wherein the amplification reagent in the third segment comprises at least one of a nucleic acid polymerase and nucleotide triphosphates.

91. **(Currently amended)** The ~~tubule~~ apparatus of claim 1, wherein the at least one substance capable of specific binding to a preselected component of a sample in the first segment specifically binds nucleic acid.

92. **(Currently amended)** The ~~tubule~~ apparatus of claim 1, wherein the third segment contains a detection reagent.

93. (Canceled)

94. **(Currently amended)** The ~~tubule~~ apparatus of claim 1, wherein the opposed wall portions of the tubule are left free of projections when the seal is broken.

95. **(Currently amended)** The ~~tubule~~ apparatus of claim 1, ~~further comprising a chamber proximal to the opening,~~ wherein the cap chamber ~~having~~ has a wall that comprises a barrier preventing liquid escape and that defines a waste cavity in fluid communication with the opening.

96. **(Currently amended)** The ~~tubule~~ apparatus of claim 1, ~~further comprising a chamber proximal to the opening,~~ wherein the cap chamber ~~having~~ has a wall that comprises a vent, and a member preventing liquid escape, and that defines a waste cavity in fluid communication with the opening.

97. **(Currently amended)** The ~~tubule~~ apparatus of claim 1, ~~further comprising a chamber proximal to the opening,~~ wherein the cap chamber ~~having~~ has a flexible membrane that prevents liquid escape, that defines a waste cavity in fluid communication with the opening, and that is deformable to increase the waste cavity volume.

98. **(Currently amended)** The ~~tubule~~ apparatus of claim 1, wherein a fourth segment distal to the third segment contains a detection reagent.

99. **(Currently amended)** The ~~tubule~~ apparatus of claim 1, wherein the substance capable of specific binding to a preselected component of the sample is, comprises, or is coupled to a solid phase substrate.

100. (**Currently amended**) The ~~tubule~~ apparatus of claim 99, wherein the wash reagent is capable of retaining the preselected component on the solid phase substrate while allowing removal of components of the sample not bound to the substrate.

101. (**Currently amended**) The ~~tubule~~ apparatus of claim 100, wherein the amplification reagent is capable of amplifying the preselected component of the sample.

102. (**Currently amended**) The ~~tubule~~ apparatus of claim 99, wherein the amplification reagent is capable of amplifying the preselected component of the sample.

103. (**Currently amended**) The ~~tubule~~ apparatus of claim 99, further comprising a fourth segment that (a) is distal to the second segment, (b) is proximal to the third segment, and (c) contains an elution reagent capable of eluting the preselect component from the substrate.

104. (**Currently amended**) The ~~tubule~~ apparatus of claim 1, wherein the amplification reagent is capable of amplifying the preselected component of the sample.

105. (**Currently amended**) The ~~tubule~~ apparatus of claim 6, wherein:

the substance capable of specific binding to the preselected component of the sample comprises silica;

the silica is coupled to magnetic beads; and

the amplification reagent comprises at least one of a primer, a nucleotide triphosphate, and an amplification enzyme.

106. (**Currently amended**) The ~~tubule~~ apparatus of claim 1, wherein the segments are prepacked with their respective contents.

Please add the following claims:

107. (**New**) The apparatus of claim 1, wherein the cap chamber contains a reagent.

108. (**New**) The apparatus of claim 1, wherein the apparatus comprises the integral tubule tensioning mechanism, and the mechanism comprises cantilever or leaf springs.

109. (**New**) The apparatus of claim 1, wherein the apparatus comprises the attachment of the tubule to the frame, and the attachment comprises at least one of a seal, a weld, an adhesive joint, and an insert-molding.

110. (**New**) The apparatus of claim 1, wherein the cap further comprises a filter that permits the free escape of gasses while retaining all liquid volumes and infectious agents in the tube.

111. (**New**) The apparatus of claim 1, wherein the cap further contains a waste cavity in fluid communication with the tubule.

Please rejoin withdrawn claims 11-13, 19-21, and 33-35.

Please renumber claims 1-4, 6-21, 24, 25, 27, 28, 30-35, 44, 45, 47, 76, 78-80, 85-92, 94-111 as claims 1-63 respectively.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nelson Yang whose telephone number is (571)272-0826. The examiner can normally be reached on 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mark Shibuya can be reached on (571)272-0806. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Nelson Yang/
Primary Examiner, Art Unit 1641